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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/676,248	09/30/2003	Peter K. Rogan	33026	5913

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EXAMINER	
POHNERT, STEVEN C	
ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/676,248	ROGAN ET AL.	
	Examiner	Art Unit	
	Steven C. Pohnert	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 October 2008*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33,43-52 and 54* is/are pending in the application.

4a) Of the above claim(s) *1-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *43-52 and 54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/28/2008 has been entered.

Sequence compliance

The application fails to comply with CFR 1.821(d), which states:

(d)Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO:" in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application.

For example, table 2 starting on page 34, contains a nucleic acid sequence that are improperly identified by "SEQ ID", not the required "SEQ ID NO:". Further the sequences disclosed in table 2 are different than those in the sequence listing. For example SEQ ID 1 of table 2 identifies a 30 nucleotide sequence, while SEQ ID NO 1 of the sequence listing is 1820 nucleotides in length. Applicant is required to correctly identify sequences by "SEQ ID NO:" and insure that sequences identified by SEQ ID NO are consistent with the sequence listing. If those sequence presented in table 2 are

fragments or primers of the full length SEQ ID NO, applicant may identify the sequence relative to the full length SEQ ID NO (i.e. nucleotides 1-30 of SEQ ID NO: 1). The applicant should review the rest of the disclosure for any other nucleic acid or protein sequences and list them in a sequence listing and identify them with a proper SEQ ID NO.

The specification and sequence listing must be amended to bring it into sequence compliance. **For any response to this office action to be fully compliant, the response has to bring the application in compliance with sequence rules.**

Claim status

This action is in response to papers filed 10/27/2008.

Claims 1-33 are withdrawn.

Claims 34-42 are canceled.

Claims 43-52 and 54 are under consideration.

The 112-1st paragraph Enablement rejection and Written description rejections of claims 43-52 and 54 have been withdrawn in light of the amendment.

The 112-2nd paragraph rejections of claims has been withdrawn in view of the amendment to the claims.

Specification

2. The disclosure is objected to because of the following informalities:

The specification is objected to for the sequence compliance issues disclosed above in the sequence compliance section. Applicant must correctly identify the nucleic acid sequences by SEQ ID NO.

Further the specification is objected in addition to the discrepancies between the SEQ ID NO: in Table 2 and the length of in the sequence listings also has discrepancies between the length of the sequences identified in the table of page 47. For example the table of page 47 identifies SEQ ID NO: 33 as 2671 bases in length, while table 2 identifies SEQ ID NO: 33 as 33 bases, and the sequence listing discloses SEQ ID NO:33 as 2533 bases in length. Applicant must correct the specification in such a manner that the length of sequences identified by SEQ ID NO: in the specification are consistent with the sequence listing or correctly identifies which nucleotides of the sequence identified by the sequence listing are encompassed by those in the specification, or corrects the disclosure in a manner that does not present new matter.

Appropriate correction is required.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 43, 45-47 are rejected under 35 U.S.C. 102(b) as being anticipated by Knight et al (Am. J. Human Genetics (2000) volume 67, pages 320-332) .

The claims are drawn to a method of detecting cytogenetic abnormalities in an individual comprising screening at least one chromosome by hybridization of a plurality of single probes of known sequences, hybridizing the probes to at least one chromosome and detecting hybridization patterns of the probes, said hybridization

patterns indicating ctyogentic abnormalities when present. The claim only requires the detection of cytogenetic abnormalities if present.

With regards to claim 43, Knight et al teaches a method of fluorescence in situ hybridization (FISH) on interphase chromosomes (see page 322, 1st column). Knight et al teaches the probes were labeled and detected. Knight et al teaches the probes and the distance from the telomere (terminal nucleotide) in table 1. Knight teaches the distance from the terminal nucleic acid was as little as 268-296 kb for 6ptel48 and teaches sequencing of the probes (see page 322, 2nd column, 1st paragraph). Knight thus teaches method of detecting cytogenetic abnormalities with a plurality of probes within 600 kb of the terminal nucleotide of the chromosome by screening at least one chromosome by hybridization with probes of known sequences, and detecting cytogenetic abnormalities when present.

With regards to claim 45, Knight teaches that 60 + probes did not cross hybridize (see tables 1 and 3).

With regards to claim 46, Knight teaches the probes had known sequences as demonstrated by the primers of table 2.

With regards to claim 47, Knight teaches the probes were nick translated. Nick translation results in a plurality of short probes, all less then 25 kb.

Response to arguments

The response on page 13 asserts that claims 43-54 are rejected under 102(b) and the instant amendment has overcome the rejection of record. First the examiner notes that claims 43, 45-47 are rejected under 102(b) not claims 43-54 as asserted.

Further the response asserts that the probes of Knight are not single copy probes as now claimed. First, MPEP 716.01(c) makes clear that "The arguments of counsel cannot take the place of evidence in the record. In re Schulze , 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long - felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant." Here, the statements regarding the probes of Knight not being "single copy" probes is argument of counsel that has not been supported by evidence.

This should not be construed as an invitation for providing evidence. As further stated in the MPEP 716.01 regarding the timely submission of evidence:

A) Timeliness.

Evidence traversing rejections must be timely or seasonably filed to be entered and entitled to consideration. In re Rothermel, 276 F.2d 393, 125 USPQ 328 (CCPA 1960). Affidavits and declarations submitted under 37 CFR 1.132 and other evidence traversing rejections are considered timely if submitted:

(1) prior to a final rejection,

(2) before appeal in an application not having a final rejection, or

(3) after final rejection and submitted

(i) with a first reply after final rejection for the purpose of overcoming a new ground of rejection or requirement made in the final rejection, or

(ii) with a satisfactory showing under 37 CFR 1.116(b) or 37

CFR 1.195, or

(iii) under 37 CFR 1.129(a).

The response asserts that pages 5 and 6 as well as page 9 of the instant specification demonstrate that the probes of Knight contain repetitive sequences as they are from YACS, PACS and BACS not single copy probes. It is noted that while page 5, lines 7-10 suggests that first generation probes were clones composed of single copy sequences interspersed with repetitive sequences, but neither pages 5 or 6 specifically teach the probes of Knight are not single copy probes. Further the response appears to be asserting that the single copy probes of the instant specification cannot contain repetitive sequences. Review of the specification did not set forth a limiting definition of a single copy probe. Further examination of page 9 suggests there are some disadvanatages of using probes from BACS, YACS and PACS but does not specifically address that the probes of Knight are not single copy probes. Further if applicant wants to exclude all repetitive sequences from the probes, many of the primers described in the instant table 2 would be excluded as they contain repetitive sequences. For example SEQ ID 1 of table 2 recites TCTGCGGCTGACCTGGCCTCCACGTCTCAC, which contains 4 repetitive CT sequences indicated by underlining.

Further the response continues that, "Thus, even though they may contain segments of single copy DNA, the presence of repetitive sequences surrounding these single copy segments means that they can be called unique, but not single copy." Thus the response apparently agrees that the sequences of Knight contain single copy

sequences. Further the instant claims do not specifically exclude the presence of repetitive sequence and the specification does not set forth a limiting definition of a single copy probe the presence of a repetitive sequence in a probe these arguments are beyond the scope of the claimed invention.

The response further asserts the presence of the “unique segments” and “single copy sequences” in the second sentence of the summary of the invention, "the present approach develops unique sequence, single copy hybridization probes" somehow differentiates the instant invention from the probes taught by Knight. These arguments have been thoroughly reviewed but are not considered persuasive as Knight discloses 60 probes that do not cross hybridize (tables 1 and 3). Thus the probes are unique and single copy sequences as they only hybridize to a single location in the genome.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 44, 48, 49-52, and 54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knight et al (A) (Am. J. Human Genetics (2000)volume 67, pages 320-332) in view of Knight (b) (Journal of Medical Genetics (2000) volume 37, pages 401-409).

The claims are drawn to a method of detecting cytogenetic abnormalities in an individual comprising screening at least one chromosome by hybridization of a plurality of probes of known sequences, hybridizing the probes to at least one chromosome and detecting hybridization patterns of the probes, said hybridization patterns indicating ctyogentic abnormalities when present. The claim only requires the detection of cytogenetic abnormalities if present.

With regards to claim 43, Knight et al teaches a method of fluorescence in situ hybridization (FISH) on interphase chromosomes (see page 322, 1st column). Knight et al teaches the probes were labeled and detected. Knight et al teaches the probes and the distance from the telomere (terminal nucleotide) in table 1. Knight teaches the distance from the terminal nucleic acid was as little as 268-296 kb for 6ptel48 and teaches sequencing of the probes (see page 322, 2nd column, 1st paragraph). Knight thus teaches method of detecting cytogenetic abnormalities with a plurality of probes within 600 kb of the terminal nucleotide of the chromosome by screening at least one

chromosome by hybridization with probes of known sequences, and detecting cytogenetic abnormalities when present.

With regards to claim 45, Knight teaches that 60 + probes did not crosshybridize (see tables 1 and 3).

With regards to claim 46, Knight teaches the probes had known sequences as demonstrated by the primers of table 2.

With regards to claim 47, Knight teaches the probes were nick translated. Nick translation results in a plurality of short probes, all less then 25 kb.

Knight (A) does not teach associating the hybridization pattern with a specific clinical abnormality (claim 44). Knight (A) does not teach correlating cytogenetic abnormalities with mental retardation or cancer (claim 48). Knight does not comparison to a genome map in order to delineate chromosome imbalance (claim 50).

However, Knight (B) et al teaches, "Chromosomal rearrangements involving the ends of chromosomes (telomeres) are emerging as an important cause of human genetic diseases. This review describes the development of first and second generation sets of telomere specific clones, together with advances in fluorescence in situ hybridisation (FISH) technology, which have made the prospect of screening for telomeric rearrangements a realistic goal. Initial FISH studies using the telomere specific clones indicate that they will be a valuable diagnostic tool for the investigation of mental retardation, the characterization of known abnormalities detected by conventional cytogenetic analysis, spontaneous recurrent miscarriages, infertility, haematological malignancies, and preimplantation diagnosis, as well as other fields of

clinical interest. In addition, they may help investigate telomere structure and function and can be used in the identification of dosage sensitive genes involved in human genetic disease.(see abstract). Knight et al further teaches, "The results suggested that at least 6% of idiopathic mental retardation might be explained by submicroscopic rearrangements involving telomeres. If true, then subtelomeric rearrangements could be the second most common cause of mental retardation after Down's syndrome. Therefore, it was important to extend these studies to include all possible telomeres and a larger sample set." Knight (b) further teaches, "The first method, the use of DNA polymorphisms, requires DNA samples from the child and both parents. When both parents are heterozygous and share no alleles, a rearrangement in the child can be inferred from the presence of only a single allele (a deletion) or the presence of three alleles (a trisomy). This technique has the advantage of being able to detect isodisomy (the inheritance of two chromosome homologues from one parent), but it is limited by the degree of polymorphism of the marker and by the need to have access to samples from both parents. Indeed, marker informativity must be very high for this technique to be efficient."

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the method of cytogenetic analysis and probes taught by Knight (A) to associate specific hybridization patterns with clinical abnormalities as taught by Knight (b), because Knight (B) teaches it would allow for better understanding of the clinical abnormalities. Knight (b) specifically teaches the such methods can be used to better understand the causes of idiopathic mental

retardation and/or cancers. It would have further been prima facie obvious to compare the sequences to standard genetic maps as Knight (B) teaches comparison of hybridization of children to parents (standard genetic maps). The artisan would have a reasonable expectation of success as Knight(A) and Knight (B) both teach method of detecting polymorphisms by FISH.

Response to Arguments

The examiner notes that Knight (A) as described above anticipates claims 43, 45-47, as discussed above. Knight (A) in view of Knight (B) renders claims 44, 48-52 and 54 obvious. The response does not provide any specific arguments to the combination of Knight (A) and Knight (B) other then reiterating the arguments to Knight (A), which has been addressed above. Thus as no specific arguments are directed to the instant combination of Knight (A) and Knight(B) the rejection is maintained.

Double Patenting

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to

be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 43-45, 49 and 51 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 3 of U.S. Patent No. 7014997 in view of Knight et al (Am. J. Human Genetics (2000) volume 67, pages 320-332) .

Although the conflicting claims are not identical, they are not patentably distinct from each other because they are co-extensive in scope.

Claim 43 of instant application is drawn to a method of screening individuals with clinical abnormalities with at least one probes. The hybridization of said probe(s) resulting in patterns indicative of cytogenetic abnormalities. Claim 3 of '997 patent teaches the detection of hybridization pattern for detection of cytogenetic abnormalities. Claim 1 of '997 patent teaches chromosome abnormalities are indicative of pathological abnormalities.

Claim 44 of instant application is drawn to associating hybridization patterns of probes with clinical abnormalities. Claim 1 of '997 patent teaches hybridization is indicative of pathological conditions.

Claim 45 of instant application is drawn to probes hybridizing to a single genomic location. Claim 1 of '997 patent teaches a nucleic acid probe complementary to a non-repetitive portion of genome. A non-repetitive portion of the genome would result in probes hybridizing to a single genomic location.

Claim 49 of instant application is drawn to detecting and delineating the extent of chromosome imbalances by comparison of probe hybridization to a standard genome map. Claim 1 of '997 patent teaches hybridization of nucleic acid of non-repetitive sequence probes with known genomic sequence coordinates. The hybridization of probes from claim 1 of '997 patent detect chromosome imbalances and since known genomic coordinates are known to delineate extent by comparison to standard genomic map.

Knight et al teaches a method of fluorescence in situ hybridization (FISH) on interphase chromosomes (see page 322, 1st column). Knight et al teaches the probes were labeled and detected. Knight et al teaches the probes and the distance from the telomere (terminal nucleotide) in table 1. Knight teaches the distance from the terminal nucleic acid was as little as 268-296 kb for 6ptel48 and teaches sequencing of the probes (see page 322, 2nd column, 1st paragraph). Knight thus teaches method of detecting cytogenetic abnormalities with a plurality of probes within 600 kb of the terminal nucleotide of the chromosome by screening at least one chromosome by hybridization with probes of known sequences, and detecting cytogenetic abnormalities when present.

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to improve the method of claims 1 and 3 of '997 with the probes within 600 kb of the terminal nucleotide of Knight. The artisan would be motivated as Knight teaches this allows accurate detection of chromosomal imbalances.

The artisan would have reasonable expectation of success as both '997 and Knight are drawn to FISH analysis.

Response to Arguments

The response provides no arguments to the instant rejection, but wishes not to address this rejection until the present claims are found allowable. The rejection is thus maintained.

Summary

No claims are allowed over prior art cited.

Conclusions

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Steven C. Pohnert whose telephone number is (571)272-3803. The examiner can normally be reached on Monday-Friday 6:30-4:00, every second Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Steven C Pohnert/
Examiner, Art Unit 1634

Steven Pohnert